

Complete Summary

GUIDELINE TITLE

Use of vinorelbine in non-small cell lung cancer.

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Use of Vinorelbine in non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Aug [online update]. Various p. (Practice guideline; no. 7-5). [26 references]

GUIDELINE STATUS

Updating activities in 1999 yielded new evidence. The findings are summarized in the August 2001 online update. Since that time, additional evidence has been uncovered during updating activities and is currently under review by the developer.

The original guideline was released in August 1996.

The guideline developer instituted a new format for their guidelines and evidence summaries: A SUMMARY of the original Practice Guideline or Evidence Summary, integrated with the most current information, replaces the ABSTRACT, RECOMMENDATION, BRIEF REPORT and EVIDENCE UPDATE.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE
 METHODOLOGY - including Rating Scheme and Cost Analysis
 RECOMMENDATIONS
 EVIDENCE SUPPORTING THE RECOMMENDATIONS
 BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
 QUALIFYING STATEMENTS
 IMPLEMENTATION OF THE GUIDELINE
 INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT
 CATEGORIES
 IDENTIFYING INFORMATION AND AVAILABILITY
 DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Non-small cell lung cancer (NSCLC)

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Management
Treatment

CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To make recommendations about the use of vinorelbine in the management of patients with NSCLC

TARGET POPULATION

Patients with non-small cell lung cancer

INTERVENTIONS AND PRACTICES CONSIDERED

Intravenous administration of vinorelbine or vinorelbine and cisplatin as a first-line chemotherapeutic agent; administration of vinorelbine as a second-line agent.

MAJOR OUTCOMES CONSIDERED

- Survival was the primary endpoint of interest.
- Response and toxicity were secondary endpoints.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE searches were done for the years January 1984 to January 1995. Search terms included non-small cell lung carcinoma, Navelbine, and vinorelbine. Articles identified by the searches, articles cited in relevant papers and reviews and proceedings of meetings (e.g., of the American Society of Clinical Oncology) were retrieved and reviewed. In addition, a selected bibliography, provided by Burroughs-Wellcome Inc, Kirkland, Quebec, Canada was reviewed.

NUMBER OF SOURCE DOCUMENTS

11 source documents

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not applicable

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

August 1996 Guideline

Early drafts of the original guideline report were reviewed by members of the Lung Disease Site Group (DSG) and the Systemic Treatment Disease Site Group (STD SG). It was suggested by the Lung DSG that all discussion of small-cell lung cancer be omitted and left for a separate guideline.

The wording of the actual evidence-based recommendation was discussed by members of the Lung Disease Site Group. It was felt that the recommendation should reflect the fact that vinorelbine is now one of several chemotherapy options available for the treatment of patients with advanced non-small cell lung cancer (NSCLC), but is not the only option available. The evidence regarding the

efficacy of vinorelbine is preliminary and the benefits noted in the Le Chevalier study (the strongest evidence) have yet to be duplicated in other trials. Until such data are available, the Lung DSG felt, as per their deliberations over the practice guideline Chemotherapy in Stage IV (Metastatic) Non-Small Cell Lung Cancer, Practice Guideline No. 7-2 (See the [National Guideline Clearinghouse \(NGC\) summary](#)), that vinorelbine may be considered as one of several chemotherapeutic agents available for use in the treatment of advanced NSCLC.

After consideration of the evidence of efficacy of vinorelbine, the group also deliberated about the potential cost implications of implementing this recommendation. A list of standard chemotherapy regimens and their approximate drug costs (1994 Canadian dollars) appears in the "Implications for Policy" subsection of the original guideline this document. The costing does not include the cost of drug administration, supportive care drugs or hospitalization if it is required for the chemotherapy delivery. These factors would also have to be considered. It should be noted that the average number of treatment cycles for vinorelbine is 3.3 with this patient population.

August 2001 Update

After reviewing new evidence that has emerged from updating activities, the Lung Cancer DSG will revise the consensus statement if applicable.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

August 1996 Guideline

There was no evidence on this topic when the original guideline report was developed.

August 2001 Update

Three reports of economic analyses of single-agent vinorelbine or vinorelbine combination chemotherapy, one reported in abstract form, are summarized below.

Evans and Le Chevalier used Statistics Canada's Population Health Model to model the cost of care per patient and the total burden of cost on the Canadian health care system for three chemotherapy strategies reported in a randomized controlled trial by Le Chevalier and colleagues (vinorelbine alone, vinorelbine-cisplatin, vindesine-cisplatin), and three additional therapies (etoposide-cisplatin, vinblastine-cisplatin and best supportive care). The most cost-effective regimen relative to best supportive care was vinblastine-cisplatin; it increased average survival by 0.27 years while reducing costs by \$3,265 per case. Vinorelbine-cisplatin increased survival to a greater degree (0.44 years/patient) but inpatient administrative costs associated with the delivery of cisplatin resulted in a cost-effectiveness ratio of \$5,551. When the cost of vinorelbine-cisplatin was adjusted to that for an outpatient setting, this combination proved to be cost-effective

relative to either etoposide-cisplatin or vinblastine-cisplatin. The authors concluded that cost and cost-effectiveness should not be barriers to the utilization of vinorelbine-cisplatin in Canada.

Hillner and Smith examined the cost-effectiveness of the three chemotherapy strategies in the randomized controlled trial by Le Chevalier et al. from an American perspective. Compared to vindesine-cisplatin, vinorelbine-cisplatin added 37 days of life at a cost of \$1,570, or \$15,500 per year of life gained. The authors concluded that the incremental cost-effectiveness of vinorelbine-cisplatin was less than most commonly accepted medical interventions.

Lappas and colleagues, in work reported in abstract form, performed a meta-analysis and cost-effectiveness analysis on data from randomized controlled trials involving patients with non-small cell lung cancer (NSCLC) treated with paclitaxel-carboplatin or vinorelbine-cisplatin. The meta-analysis showed no statistically significant differences between the total response rates for the regimens. Assuming six treatment cycles of each regimen, the total expected costs of the paclitaxel-carboplatin and vinorelbine-cisplatin regimens were \$19,322 and \$20,790 (\$ United States), respectively.

The Lung Cancer Disease Site Group is reviewing new evidence that has emerged from review and updating activities.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey consisting of nine questions asking for comments on the quality of the evidence-based recommendation (EBR), and whether the recommendation should serve as a practice guideline. Written comments were invited. Follow-up reminders were sent at four weeks (telephone) and six weeks (mail). Results were reviewed by the Lung Cancer DSG.

The Coordinating Committee of the Cancer Care Ontario Practice Guidelines Initiative externally evaluated the practice guideline for final approval.

This practice guideline was also reviewed by two external reviewers prior to publication in the journal Cancer Prevention and Control.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse: Updating activities in 1999 yielded new evidence. The findings are summarized in the August 2001 online update. Since that time, additional evidence has been uncovered during updating activities and is currently under review by the developer. The original

recommendations, released August 1996 and recorded below, currently remain unchanged.

- Evidence from randomized controlled trials supports the use of vinorelbine as an option for the first line treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC).
- The use of vinorelbine as a single agent, or in combination with cisplatin, depends on anticipated tradeoffs between the expected symptomatic benefits from a higher response rate with the combination and the increased toxicity. Evidence for a possible survival advantage for the combination of vinorelbine/cisplatin over vinorelbine alone is conflicting.
- There is insufficient evidence at the present time to advocate the use of vinorelbine in previously treated patients who have recurrent or progressive disease.
- Similarly, there is insufficient evidence at the present time to advocate the use of vinorelbine as adjuvant or induction therapy for patients with stage I, II or early stage III disease.
- The enrolment of patients with non-small cell lung cancer in clinical trials is encouraged.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Only evidence from randomized controlled trials (RCTs) and Phase II studies was evaluated. Six RCTs and 5 phase II studies were reviewed and are discussed in this guideline. Of the 6 RCTs, 3 had been fully published at the time of guideline issuance.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Vinorelbine, either as a single agent or in combination with cisplatin, produces higher response rates (12-37%) than other single agent vinca alkaloids (10-20%) in patients with previously untreated NSCLC. Two of 3 RCTs that reported survival differences demonstrated a survival benefit for previously untreated patients with NSCLC when treated with vinorelbine in combination with cisplatin as compared with patients treated with either vindesine plus cisplatin ($p=0.04$) or leucovorin plus 5-FU ($p=0.03$). The third study reported no statistically significant difference between patients treated with vinorelbine alone and those receiving vinorelbine plus cisplatin.

POTENTIAL HARMS

The major toxicities are hematologic. Neutropenia is the dose-limiting toxicity. However, there is less neurotoxicity than with other vinca alkaloids (e.g., vindesine) and less nausea and vomiting than with other active agents used in the treatment of NSCLC.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

The evidence regarding the efficacy of vinorelbine is preliminary and the benefits noted in the strongest evidence have yet to be duplicated in other trials.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Practice Guideline Initiative (CCOPGI). Use of Vinorelbine in non-small cell lung cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Aug [online update]. Various p. (Practice guideline; no. 7-5). [26 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 Aug 15 (new information released online August 2001)

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

The Provincial Lung Disease Site Group in conjunction with the Systemic Treatment Program Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The Lung Disease Site Group and the Systemic Treatment Program Committee comprise medical and radiation oncologists, pathologists, surgeons, epidemiologists, pharmacists, nurses, a psychologist, a medical sociologist, and administrators. No consumers participated in the development of this guideline.

Members of the Lung Disease Site Group (DSG): Dr. William K. Evans (Chair), Medical Oncologist; Dr. Yasmin Alam, Medical Oncologist; Dr. Barbara Campling, Medical Oncologist; Dr. Dean Chamberlain, Pathologist; Dr. Gail Darling, Surgeon; Dr. Peter Dixon, Radiation Oncologist; Dr. Ron Feld, Medical Oncologist; Dr. Brian Findlay, Medical Oncologist; Dr. Glen Goss, Medical Oncologist; Dr. Ian Graham, Medical Sociologist; Dr. Neill Iscoe, Medical Oncologist; Dr. Walter Kocha, Medical Oncologist; Dr. Arnost Kolin, Pathologist; Dr. Jaro F. Kotalik, Radiation Oncologist; Dr. Andreas Laupacis, Epidemiologist; Dr. Catherine A. Lochrin, Radiation Oncologist; Dr. Diane Logan, Medical Oncologist; Dr. Pedro Lopez, Medical Oncologist; Dr. Richard Malthaner, Surgeon; Dr. John Miller, Surgeon; Ms. Toni Newman, Project Coordinator, Practice Guidelines Resource Group; Dr. Gordon Okawara, Radiation Oncologist; Dr. Larry Paszat, Radiation Oncologist; Dr. Ken Reid, Surgeon; Dr. James J. Rusthoven, Medical Oncologist; Dr. Scott Sellick, Psychologist; Dr. Frances Shepherd, Medical Oncologist; Dr. David Stewart, Medical Oncologist; Dr. Mark Vincent, Medical Oncologist; Dr. Georg Wenckebach, Pathologist; Dr. Stanley Yu, Radiation Oncologist

Members of the Systemic Treatment Program Committee: Dr. V. Bramwell, Chair, Medical Oncologist; Ms. E. Anderson, RN; Mr. L. Broadfield, Pharmacist; Ms. F. Charbonneau, Pharmacist; Ms. M. Colquhoun, Pharmacist; Dr. R. Feld, Medical Oncologist; Dr. B. Findlay, Medical Oncologist; Dr. S. Fine, Medical Oncologist; Dr. N. Iscoe, Medical Oncologist; Dr. M. Moore, Medical Oncologist; Mrs. M. Nefsky, Director of Provincial Programs, Corporate Office, OCTRF; Mrs. S. Palmer-Wickham, RN; Dr. J. Pater, Medical Oncologist; Dr. J. Rusthoven, Medical Oncologist; Dr. D. Stewart, Medical Oncologist

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Lung Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

Updating activities in 1999 yielded new evidence. The findings are summarized in the August 2001 online update. Since that time, additional evidence has been uncovered during updating activities and is currently under review by the developer.

The original guideline was released in August 1996.

The guideline developer instituted a new format for their guidelines and evidence summaries: A SUMMARY of the original Practice Guideline or Evidence Summary, integrated with the most current information, replaces the ABSTRACT, RECOMMENDATION, BRIEF REPORT and EVIDENCE UPDATE.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Use of vinorelbine in non-small cell lung cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 1996 Aug (updated online 2001 Aug).

Electronic copies: Available from the [Cancer Care Ontario Web site](#).

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on January 5, 1999. The information was verified by the guideline developer as of February 22, 1999. This summary was updated by ECRI on April 12, 2002.

COPYRIGHT STATEMENT

This NGC summary is based on the original guideline, which is subject to the guideline developer's copyright restrictions. Please refer to the [Copyright and Disclaimer Statements](#) posted at the Cancer Care Ontario Web site.

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at <http://www.guideline.gov/about/inclusion.aspx>.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

© 1998-2006 National Guideline Clearinghouse

Date Modified: 10/9/2006

